11:30 a.m.

810-3 Prognostic Significance of B-Type Natriuretic Peptide in the Hemodialysis Patient

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Background: Although the population of maintenance hemodialysis has been rapidly increasing and cardiovascular complications are their major cause of death, it has not been clarified whether the circulating hormonal factors relate the mortality in these patients.In the present study, we aimed to determine the prognostic power of plasma natriuretic peptides in patients on maintenance hemodialysis, comparing with that of cardiac function and the frequency of arrhythmias. The primary endpoint was all-cause mortality.
Methods: Measurements of A-type and B-type plasma natriuretic peptides (ANP, BNP), echocardiography, and 24-hour ambulatory monitoring of ECG were performed in 724 consecutive patients with maintenance hemodialysis (57 ± 13 yr). Plasma natriuretic peptides were measured immediately before hemodialysis; ambulatory monitoring of ECG was performed including a period of hemodialysis in all the patients.
Results: After two years of prospective follow-up, 88 deaths occurred. The plasma BNP level was markedly higher in non-survivors than in survivors (mean ± SD;732 ± 860 vs 371 ± 434 pg/ml, p<0.0001). Plasma ANP level was also higher in non-survivors than in survivors (229 ± 205 vs. 162 ± 214 pg/ml, p<0.0001). Left ventricular ejection fraction was lower (62 ± 14 vs. 66 ± 11 %, p=0.0012) and premature atrial complexes during 24 hours were more frequent in nonsurvivors as compared to those in survivors. In the univariate Cox proportional hazards model, all of these indices were found to be significant prognostic indicators for survival. However, only high levels of plasma BNP revealed to be a significant independent predictor when these indices were entered into a multivariate analysis. Kaplan-Meier survival curves demonstrated a survival rate of 59 % for patients with plasma BNP>292 pg/ml (median value) and 81 % for those with plasma BNP < 292 pg/ml, showing a significant difference in survival (p<0.0001).
Conclusions: These findings indicate that plasma BNP is the most useful index among hormonal and cardiovascular variables for assessing the mortality in patients with maintenance hemodialysis.

11:45 a.m.

810-4 Pexelizumab, a C5 Complement Inhibitor, Reduces 30-Day Mortality in Patients Undergoing Coronary Artery Bypass Surgery or Receiving Reperfusion Therapy for Acute Myocardial Infarction

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Background: Complement activation may contribute to myocardial injury in patients experiencing ischemia/reperfusion either from coronary artery bypass surgery (CABG) with cardiopulmonary bypass or from reperfusion therapy (primary angioplasty or thrombolysis) for acute myocardial infarction (AMI). Pexelizumab, a single-chain monoclonal antibody against C5, given as a bolus and a 20-24hr infusion, was compared, double blind, with placebo in 3,631 CABG (phase II: 606; phase III: 3,025) and in 1,274 AMI (primary angioplasty: 643; thrombolysis: 631) patients. We performed an intention-to-treat analysis of all-cause mortality at 30 days in the total population studied.
Results: Number of patients, number of deaths, relative risks (RR) and 95% confidence intervals (CI) in the different studies and in the total population are shown below.
Conclusion: When compared with placebo, pexelizumab was associated with a significant reduction in 30-day mortality in the total population studied. These encouraging results support further studies with pexelizumab in inflammatory mediated disease states in which complement activation plays a pathophysiological role.

		Placebo	Pexelizumab	RR (95% CI)	p
CABG	phase II	7/306	3/300	0.44 (0.11 – 1.67)	0.340
	phase III	51/1508	41/1517	0.70 (0.48 – 1.12)	0.162
AMI	primary angioplasty	16/315	7/328	0.42 (0.18 – 1.01)	0.055
	thrombolysis	28/316	23/315	0.82 (0.49 – 1.40)	0.560
All Trials		102/2442	71/2460	0.69 (0.51 – 0.93)	0.016

Noon

810-5 Use of Either Metformin or Thiazolidinedione Is Associated With Improved Survival Among Patients With Type 2 Diabetes From a Registry of 16,203 Diabetic Patients

Farangis Lavasani, Joseph B. Muhlestein, Dalton Einhorn, Robert R. Pearson, Heath U. Jones, Benjamin D. Horne, Tami L. Bair, Heidi Thomas, Dale G. Renlund, Donald L. Lappe', Jeffrey L. Anderson, LDS Hospital, Salt Lake City, UT, Sankyo Pharma, Parsippany, NJ

Background: Type II diabetes mellitus (DMII), mainly a disease of insulin resistance, is a known risk factor for mortality. Management of hyperglycemia associated with DMII is possible through a variety of medications including insulin supplying [exogenous insulin (I) or sulfonylureas (SU)] or sensitizing [(metformin (MF) or thiazolidinediones (TZD)] agents. It is unclear how these agents affect survival. The objective of this study was to evaluate the incidence of all-cause mortality among patients (pts) with DMII based on the type of diabetic medications prescribed.
Methods: An observational registry of 16,203 pts with a DMII admission ICD-9 code was developed during the decade between January 1, 1992 and December 31, 2001 and pts followed until July 1, 2002. Pt baseline clinical (including baseline glycosylated hemoglobin A1C) and demographic characteristics were recorded and Cox regression controlled for these multiple covariates. Adjusted all-cause mortality associated with the use of each diabetic medication class was then compared with that of the entire population not taking that specific medication.
Results: Information regarding discharge prescriptions was available on 8,004 pts. Of these, 88% received I, 43% received SU, 20% received MF, and 4% received TZD with many pts receiving multiples of these medications. Use of TZD (adjusted HR = 0.60 [95% confidence interval (CI) = 0.40, 0.91], p = 0.015) and MF (adjusted HR=0.74 [0.62, 0.87], p<0.001) were associated with significantly lower mortality than SU (adjusted HR=0.87 [0.78, 0.96], p=0.006) or I (adjusted HR=2.3 [2.1, 2.5], p<0.001). Insulin therapy was associated with an especially worse outcome compared to no insulin therapy (adjusted HR 3.0, p<0.001). Baseline glycosylated hemoglobin did not affect the results of this study.
Conclusion: In this large observational study of patients with DMII, the insulin sensitizing agents TZD and MF were associated with better survival outcomes than insulin-providing therapies (SU, I). The possibility that this represents a causal relationship deserves testing in prospective randomized clinical trials.

ORAL CONTRIBUTIONS

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Inflammation, Insulin Resistance, Endothelial Function, and Cardiovascular Risk

Monday, March 08, 2004, 11:00 a.m.-12:15 p.m.
Morial Convention Center, Room 207

11:00 a.m.

812-1 C-Reactive Protein, the Metabolic Syndrome, and Prediction of Cardiovascular Events in the Framingham Offspring Study

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Background: Inflammation (assessed by C-reactive protein; CRP), and the Metabolic Syndrome (MetS; by the NCEP-ATP III definition), have been linked to the development of cardiovascular disease (CVD), but population-based data in men and women are limited.
Methods: Persons with diabetes or CVD at baseline were excluded. We analyzed the cross-sectional relations of CRP to the MetS in 3037 Framingham Heart Study subjects (1681 women, mean age 54 years), and used age-, sex-, and multivariable-adjusted models to assess the utility of CRP and the MetS to predict incident CVD (cardiovascular death, myocardial infarction, unstable angina, stroke or TIA) over 8 years of follow-up.
Results: The MetS (>3 of 5 traits) was present in 24% of subjects; mean CRP levels for those with 0, 1, 2, 3, 4 or 5 MetS traits were 0.3, 0.7, 1.2, 2.3, 2.7 and 4.1 mg/L respectively (age-adjusted trend p<0.0001). Among persons with >2 traits of the MetS, CRP levels were higher in women than in men (p<0.02). CRP levels were higher in persons with elevated BMI, waist circumference, abnormal CVD risk factor levels, and fasting hyperinsulinemia. There were 189 CVD events during follow-up; MetS and baseline CRP were individually related to CVD events (age-sex-adjusted HR (95% CI): 2.1 (1.5-2.8) for MetS, and 2.2 (1.4-3.5) for CRP comparing persons in the highest and lowest quartiles). Greater risk of CVD persisted for MetS and CRP even after adjustment in a model including age, sex, MetS (HR (95% CI): 1.8 (1.4-2.5)), and CRP (1.9 (1.2-2.9) comparing highest and lowest quartiles). The c-statistic associated with the age-sex-adjusted model that included CRP was 0.72, for the adjusted model with MetS was 0.74, and for the adjusted model including CRP and MetS was 0.74.
Conclusions: Elevated CRP levels are related to insulin resistance and to the presence of the MetS. Higher CRP levels in women compared to men with the MetS might help to explain the greater increase in CVD risk experienced by women with diabetes and prediabetes. Although discrimination of subjects at risk for CVD events using both MetS or CRP is not better than using either phenotype alone, both CRP and MetS are independent predictors of new CVD events.